IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Atty. Docket: FISHMAN9B

In re Application of:	)	Conf. No.: 6424
Pnina FISHMAN et al	)	Art Unit: 1645
Appln. No.: 10/763,190	)	Examiner: Z.C. Howard
Filed: January 26, 2004	)	Washington, D.C.
For: DIAGNOSTIC MARKERS FOR THERAPEUTIC TREATMENT	)	

DECLARATION

Honorable Commissioner for Patents
U.S. Patent and Trademark Office
Randolph Building, Mail Stop Amendments
401 Dulany Street
Alexandria, VA 22314

Sir:

We, the undersigned Pnina Fishman and Kamel Khalili hereby declare and state as follows:

We are the inventors of U.S. application no. 09/788,477, which was published as U.S. 2002/0115635 on August 22, 2002. The application date was February 21, 2001. This application claims a method for therapeutic treatment to modulate GSK-3β activity in cells by administering an adenosine A1 receptor ligand, an adenosine A2 receptor ligand or an adenosine A3 receptor ligand, or a combination thereof. We also claimed a pharmaceutical composition for achieving this therapeutic effect. The claimed subject matter was the

co-invention of the undersigned Pnina Fishman and Kamel Khalili.

In the specification of said application, we included an Example 2 relating to the effect of Cl-IB-MECA on the Wnt pathway in colon carcinoma-bearing mice. Such mice were treated with the active agent, and 30 days later the mice were sacrificed and tissue samples from the colon carcinoma foci were harvested and analyzed for the expression of β-catenin and cyclin D1. It was shown that there was a decrease in the level of β-catenin, cyclin D1 and c-myc, thus providing evidence for the participation of the Wnt signaling pathway in Cl-IB-MECA-mediated melanoma and colon carcinoma cell growth *in vitro*.

The concept of monitoring the effectiveness of an administered agent that interacts with the A3 adenosine receptor treatment of a disease state by withdrawing a sample of these cells or tissue, detecting the level of a physiological parameter, which is an element associated with A3AR signal transduction, and comparing that level with a control level, with a difference in level of the physiological parameter from the control being indicative of the effectiveness of the treatment against the disease state, was not invented by the undersigned Pnina Fishman and Kamel Khalili. This concept had been previously invented by the

inventive entity of Pnina Fishman, Lea Madi and Sara Bar-Yehuda. This previous invention had been communicated to the undersigned inventive entity, and it was used as an example in the above-identified application in order to prove the effectiveness of our invention. However, as indicated above, that disclosure was not intended to be a disclosure of our invention, but it is actually a disclosure of the invention of the Fishman, Madi and Bar-Yehuda inventive entity.

The undersigned declare further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

August 1st, 2005
Date

P. Fishman
Pnina Fishman

Date

Kamel Khalili

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_____ _____

Date Pnina Fishman

Aug. 1. 05 _____

Date Kamel Khalili